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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,177	TENGLER ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-61* is/are rejected.

7)☒ Claim(s) *4,23 and 44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 9/5/2006, have been fully considered and are persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. Unfortunately, upon further consideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1 and 4-61 are currently pending and are the subject of this Office Action.

Election/Restrictions

The Election of Species Requirement set forth in the Office Action mailed 6/2/2006 is hereby withdrawn. All species of the first active and second active are presently under examination.

Claim Objections

Claims 4, 23 and 44 are objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

In the instant case, claims 1, 20 and 40, from which claims 4, 23 and 44 respectively depend, recite "[A]n enveloped pharmaceutical composition" in line 1 of each respective claim. Applicants define the term "enveloped pharmaceutical" to mean "a capsule, a suppository, a gel

cap, a softgel, a lozenge, a sachet or even a fast dissolving wafer" (page 7, ¶ [0025]). Thus, packing the first and second actives into a capsule, a suppository, a gel cap, a softgel, a lozenge, a sachet or a fast dissolving wafer as recited in claims 4, 23 and 44 does not further limit claims 1, 20 and 40 because an enveloped pharmaceutical already requires this limitation when read in light of the specification.

Claim Rejections - 35 USC § 112 (Second Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 61 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the instant case, claim 61 has been amended to recite, "...a second active for extended release on a carrier selected from the group consisting of..." The claim is indefinite because it reads as the carrier being selected from the recited Markush group. However, the species recited in the Markush group appear to be second actives, not carriers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 9, 12-23, 28-30, and 32-39 rejected under 35 U.S.C. § 102(a) as being anticipated by Davis *et al.* (US 2003/0049318 A1; Published Mar. 13, 2003) (prior art of record).

The instant claims are drawn to enveloped pharmaceutical compositions comprising a first active for immediate release and a second active for extended release wherein the first and second actives are disposed on separate carriers (*e.g.* Claim 1). Dependent claims recite that the first active is guaifenesin and the second active is phenylephrine.

Davis *et al.* disclose immediate and sustained release formulations of guaifenesin and additional drug ingredients, including antitussives (*e.g.* codeine) and decongestants (*e.g.* phenylephrine) (Abstract; page 4, ¶ [0045]). Said formulations relate to sustained release preparations in the form of capsules having beads or granules of both immediate release formulation and beads or granules of sustained release formulation (page 2, ¶ [0019]). The reference thus teaches the limitations of claims 1, 4, 9, 12-17 and 19-23, 28-30 and 32-39.

Applicant has argued that Davis *et al.* teach a "dumb pill" with immediate release layer and a sustained release layer. Examiner respectfully submits that applicants are attempting to limit Davis to a preferred embodiment (see page 4, ¶ [0043]) wherein "bi-layered tablets or capsules" are taught). Davis *et al.* explicitly contemplate capsules (*i.e.* enveloped composition) having a combination of "beads or granules of immediate release formulation and beads or granules of sustained release formulation" (*i.e.* disposed in separate carriers) (page 4, ¶ [0043]). They go on to state that the invention will be described in detail in the context of the bi-layer

tablet embodiment (*id.*). Thus, it is not clear how the compositions of the instant invention are patentably distinct from the compositions taught in Davis *et al.*

"Granules" (page 4, ¶ [0043]) of immediate release guaifenesin read on guaifenesin "in a powder form" as instantly claimed *(e.g.* claim 10). The formulations of the invention can also include other excipients (page 4, ¶ [0050]), thus anticipating claims 18 and 38.

With respect to instant claims 20-23, 28-30 and 32-39, the limitation wherein "the first active effects a physiological result that improves the physiological action of the second active upon extended release" is inherently anticipated by Davis *et al.* because the reference teaches identical compositions to those instantly claimed. As such, the compositions and the physiological effects of those compositions are inseparable.

The reference thus discloses capsules containing both immediate release and sustained release formulations that contain guaifenesin and phenylephrine.

Claims 1, 4, 9, 11 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Blume *et al.* (U.S. Patent No. 6,372,252; Issued April 16, 2002) (cited by applicants).[1]

The instant claims are drawn to enveloped pharmaceutical compositions comprising a first active for immediate release and a second active for extended release wherein the first and second actives are disposed on separate carriers (*e.g.* Claim 1). It is noted that the instant claims recite that the second active is selected from the group consisting of a decongestant, an antihistamine, an expectorant, an antitussive and mixtures thereof (e.g. claim 1). Thus, the

[1] Blume *et al.* was issued less than a year before the filing date of the instant application. The reference qualifies as prior art under 35 U.S.C. § 102(e) because the application was filed on April 28, 2000.

claims read on a composition comprising guaifenesin in both immediate and sustained release formulations.

Blume *et al.* teach sustained release formulations of guaifenesin (Abstract). Although the reference exemplifies a bi-layer tablet of guaifenesin in immediate and sustained release formulations, capsules containing immediate and sustained release beads of guaifenesin are also contemplated (col. 3, lines 56-60). The reference also teaches a dose of 211 mg of guaifenesin in the immediate release formulation (col. 16, Example 5). The compositions taught in Blume *et al.* can also include other inactives (see Examples).

The reference thus teaches the limitation of claims 1, 4, 9, 11 and 18.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1 and 4-61 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Devane *et al.* (U.S. Patent No. 6,228,398; Issued May 8, 2001) in view of Dang *et al.* (U.S.

Patent No. 6,462,094; Issued Oct. 8, 2002) (cited by applicants) and Davis *et al.* (US 2003/0049318 A1; Published Mar. 13, 2003) (prior art of record).[2]

The instant claims are drawn to enveloped pharmaceutical compositions comprising a first active for immediate release and a second active for extended release wherein the first and second actives are disposed on separate carriers (*e.g.* Claim 1). Applicants state that the problem to be solved in the prior art at page 4, ¶ [0013]:

> "It has been found, however, that the present methods fail to provide an efficacious amount of a first active ingredient in an immediate release form and a second active that is provided as an extended release formulation that takes advantage of the pharmacological effect of the immediate release active to maximize the efficiency of the delivery and pharmacological action of the second active. Yet another problem is that certain drugs affect the release profile of a second drug that is being provided in a single dose. The present invention solves these problems in the art."

To solve the prior art problems as presented in the instant case, one skilled in the art would need the means to formulate an enveloped composition comprising a first active for immediate release and a second active for extended release (wherein the first and second actives are provided on separate carriers). The skilled artisan would also need a motivation to formulate such a composition with guaifenesin and phenylephrine. Examiner herein presents a *prima facie* case of why the instantly claimed compositions would have been obvious to one of ordinary skill in the art.

Devane *et al.* disclose multi-particulate modified release compositions that deliver active ingredients in a pulsed or bimodal manner (Abstract). One object of the invention is to provide a

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[2] Devane *et al.* qualifies as prior art under 35 U.S.C. § 102(b). Dang *et al.* and Davis *et al.* qualify as prior art under 25 U.S.C. § 102(a).

multi-particulate modified release composition in which a first portion of the active ingredient is released immediately upon administration and a second portion is released rapidly after an initial delay period (*i.e.* extended release) in a bimodal manner (col. 3, lines 51-56). The first and second components are disposed on separate carriers (*i.e.* particles) (col. 4, lines 10-14) and can be the same or different (col. 4, lines 14-16). The active ingredient-containing particles of the second component are coated with a modified release coating (col. 4, lines 15-18). In a preferred embodiment, the first component is an immediate release component (col. 4, lines 24-26). The patentees further contemplate combined therapy. For example, when the first and second components are different, an enhancer compound or a sensitizer compound in another component of the composition may accompany the drug compound present in one component in order to modify the bioavailability or therapeutic effect of the drug compound (col. 6, line 64 to col. 7, line 8). By modifying the excipients or coatings of the particles, the time-release characteristics of the active ingredient from each component may be varied (col. 7, lines 38-42). The invention of Devane *et al.* is exemplified in a preferred embodiment as recited at col. 8, lines 22-29) (emphasis added):

> In a preferred embodiment, the multi-particulate modified release composition according to the present invention has an immediate release component and at least one modified release component, the immediate release component comprising a first population of active ingredient containing particles and the modified release components comprising second and subsequent populations of active ingredient containing particles.

The multi-particle modified release composition according to the reference may be incorporated into any suitable dosage form, including filling into capsules, such as hard or soft gelatin capsules or compressed into mini-tabs and subsequently filled into capsules (col. 10, lines 15-

27). The compositions taught in the reference can also include one or more inactives as instantly claimed (Table 2). The reference also discloses the instantly claimed dissolution rates recited in claims 5-8, 24-27 an 40 (col. 12, lines 15-21 and Table 3).

Thus, while Devane *et al.* provide the means to formulate an enveloped composition of a first active for immediate release and a second active for extended release, they do not teach that the first active comprises guaifenesin or that the second active comprises phenylephrine. Devane *et al.* also do not teach that the second active is selected from the group consisting of a decongestant, an antihistamine, an expectorant, or an antitussive.

Dang *et al.* is provided as evidence that guaifenesin and phenylephrine compositions were known in the art at the time the present invention was made. The patentees disclose that guaifenesin has an expectorant action, which increases the output of respiratory tract fluid by reducing adhesiveness and surface tension (col. 2, lines 3-5). The compositions described in Dang *et al.*, comprising guaifenesin and phenylephrine, provide the immediate expectorant action of guaifenesin and the prolonged decongestant action of phenylephrine (col. 2, lines 11-13). The compositions may be prepared for oral administration in the form of powders, capsules, elixirs, syrups and the preferred forms of tablets or suspensions (col. 2, lines 15-17). The reference thus provides one skilled in the art with the motivation to formulate a composition comprising guaifenesin and phenylephrine wherein the patentees state that the combination produces a composition possessing "sympathomimetic decongestant and expectorant properties superior to the use of either one of the compounds alone" (col. 1, line 65 to col. 2, line 3).

Davis *et al.* disclose immediate and sustained release formulations of guaifenesin and additional drug ingredients, including antitussives (*e.g.* codeine) and decongestants (*e.g.*

phenylephrine) (Abstract; page 4, ¶ [0045]). Said formulations relate to sustained release preparations in the form of capsules having beads or granules of both immediate release formulation and beads or granules of sustained release formulation (page 2, ¶ [0019]). The reference thus teaches the limitations of claims 1, 4, 9, 12-17 and 19-23, 28-30 and 32-39. Davis *et al.* explicitly contemplate capsules (*i.e.* enveloped composition) having a combination of "beads or granules of immediate release formulation and beads or granules of sustained release formulation" (*i.e.* disposed in separate carriers) (page 4, ¶ [0043]). They go on to state that the invention will be described in detail in the context of the bi-layer tablet embodiment (*id.*). "Granules" (page 4, ¶ [0043]) of immediate release guaifenesin read on guaifenesin "in a powder form" as instantly claimed *(e.g.* claim 10). The formulations of the invention can also include other excipients (page 4, ¶ [0050]), thus disclosing the limitations of claims 18 and 38. The reference thus discloses capsules containing both immediate release and sustained release formulations that contain guaifenesin and phenylephrine.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

In the instant case, the prior art discloses compositions comprising guaifenesin and phenylephrine, both in immediate release and immediate/sustained release formulations. The prior art also provides methods for formulating drug compositions comprising immediate release

beads and sustained released beads in an enveloped composition having the dissolution profiles instantly claimed. The prior art differs from the instant claims in that no single reference discloses enveloped compositions comprising an immediate release agent (*e.g.* guaifenesin) and a sustained release agent that is a decongestant (*e.g.* phenylephrine), an antihistamine, an expectorant, or an antitussive disposed on separate carriers with the dissolution profiles instantly claimed. The level of ordinary skill in the art is that of an M.D., Ph.D. or pharmacist.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the multi-particle modified release compositions disclosed in Devane *et al.* by providing immediate release guaifenesin and extended release phenylephrine particles. Dang *et al.* and Davis *et al.* both provide the motivation to do so. Dang *et al.* disclose that combined guaifenesin/phenylephrine compositions provide immediate decongestant action of guaifenesin and extended expectorant action of phenylephrine. Davis *et al.* disclose compositions comprising immediate release guaifenesin and sustained release guaifenesin with additional drug ingredients, including the instantly claimed antitussives and decongestants (*e.g.* phenylephrine). Although Davis *et al.* exemplify bi-layer tablet formulations, capsules containing immediate release and sustained release beads are also disclosed. It is noted that the dissolution profiles disclosed in Davis *et al.* for sustained release formulations are longer than those instantly claimed. However, it well within the level of ordinary skill in the art to modify release profiles of drugs by changing the sustained release layer as evidenced by Devane *et al.*

Thus, one skilled in the art had the means (Devane *et al.*) and the motivation (Dang *et al.* and Davis *et al.*) to formulate an enveloped composition comprising an immediate release first active and a sustained release second active wherein the first and second actives are disposed on

separate carriers and the first active is guaifenesin and the second active is phenylephrine. Applicants have provided no evidence of unexpected results with the instantly claimed compositions of guaifenesin and phenylephrine.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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December 4, 2006

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